

THE BONNEVIE-ULLRICH SYNDROME

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Turner's syndrome, the association of webbing of the neck, cubitus valgus and infantilism, is well recognized. Much less attention, however, has been paid to a condition occurring in infancy characterized by symmetrical webbing of the neck and lymphangiectatic oedema of the extremities as well as other features, and is termed the Bonnevie-Ullrich syndrome. This condition has been extensively studied on the continent of Europe, and Ullrich (1949) now believes that the bilateral symmetrical form of this condition is identical with Turner's syndrome.

There appears to be no report of cases of the Bonnevie-Ullrich syndrome in Great Britain although James (1952) has described a case of Turner's syndrome in a male infant. The following case therefore is presented in the hope that further interest may be stimulated in this unusual congenital malformation.

Case Report

M.V., a girl, was born at term in a Stirlingshire maternity home on May 21, 1953, after an uneventful pregnancy. The birth weight was 3.6 kg. (8 lb.). She was the third child of healthy, unrelated parents. The family history appeared irrelevant.

After five weeks of normal progress she began to vomit frequently, and, because of the projectile nature of these vomits, she was admitted to the Royal Hospital for Sick Children, Edinburgh, on July 28, aged 2 months.

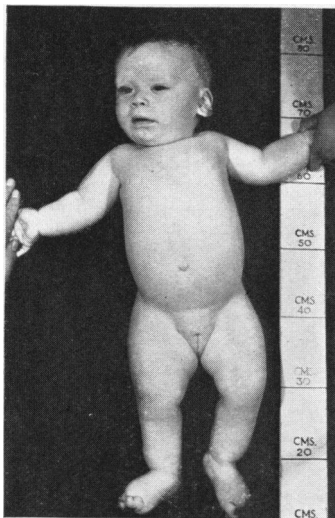


FIG. 1.—M.V., aged 8 months.

The presence of congenital hypertrophic pyloric stenosis was confirmed and the condition was relieved successfully by Rammstedt's operation on August 4.

It was noted on admission that she was a well nourished healthy looking infant despite the vomiting. In addition, certain unusual features were present. She had well developed epicanthic folds, a low nasal bridge and a cavernous haemangioma which deformed the lobe of the left ear (Fig. 1). There was latent webbing of the neck which could be easily drawn out (Fig. 2) and the skin of the upper back was unusually loose. There was a low nuchal hairline. An outstanding feature was the marked non-pitting oedema of the feet (Fig. 3) and, to a lesser extent, of the hands. The nipples were small and widely separated. Cubitus valgus deformity was present. The

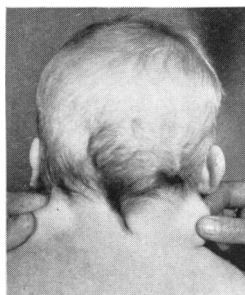


FIG. 2.

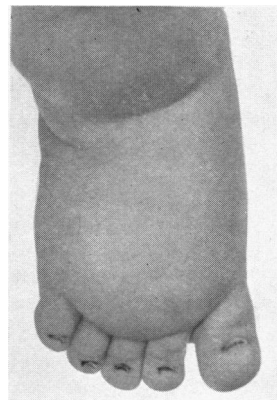


FIG. 3.

finger and toe nails were deformed. Muscle tone and joint motility were considered normal. No evidence of congenital heart disease was found, the femoral pulses, the heart outline radiologically and the electrocardiogram being normal.

The external genitalia were normal for the child's age.

Radiology showed normal skull films without increased digital impressions. The spine views showed no vertebral anomalies. The long bones appeared to be broad at the epiphyses but assessment at this age was difficult. The extremities showed no bony abnormality.

The blood examination, the plasma proteins and the urine were all normal and the Wassermann reaction was negative.

The child has been seen at regular intervals since the operation for pyloric stenosis and her progress has been normal. On February 1, 1954, she was admitted for further assessment. The oedema was still well marked although less tense and there had been no change in the latent webbing of the neck. The child's measurements at the age of 8 months were as follows: Length, 65.5 cm. (25½ in.); sitting height, 42 cm. (16½ in.); occipito-frontal circumference, 45 cm. (17¾ in.); chest circumference, 49 cm. (19¼ in.); abdominal circumference, 46.5 cm. (18¼ in.); weight, 8.8 kg. (19½ lb.).

An estimation of the 24-hour excretion of urinary gonadotrophins showed less than 6 mouse units of the follicle-stimulating hormone.

Discussion

The combination of webbing of the neck and lymphangiectatic oedema was commented upon by Ullrich in 1930. He described a 'Typisches Kombinationsbild Multipler Abartungen' which included in addition deformities of the ears, hypoplasia of the nipples, syndactyly, dystrophic nails, muscle defects and motor disturbances in the cranial nerve area. His report included four cases observed personally and 15 from the literature.

In 1938, after studying the work of Bonnevie (1934), which demonstrated the formation of multiple anomalies in an abnormal strain (my) of the house mouse, by 'wandering blebs' of cerebrospinal fluid acting in the early embryo, Ullrich postulated that such a mechanism might also be responsible for the syndrome which he had described. He quoted reports of 'stillborn foetuses showing massive oedema of the neck region of a form like that occurring in "my" mouse embryos'.

The condition became known as the Bonnevie-Ullrich syndrome, and a number of cases have been reported in German, Swiss, French and Italian journals and were reviewed by Rossi and Cafisch (1951).

Meanwhile in 1938, Turner in America had described a syndrome characterized by the triad of infantilism, congenital webbed neck and cubitus valgus. As this was subsequently considered primarily an endocrine disorder, further study of the syndrome was directed principally at the associated hypogonadism.

After the Second World War when the interchange of scientific knowledge between America and the European continent was resumed Ullrich (1949) reassessed his original conception of the Bonnevie-Ullrich syndrome, and he concluded that it could no longer be reconciled with an unqualified theory of wandering cerebrospinal fluid blebs.

The symmetrical form, which was characterized by bilateral webbing of the neck, showed the most

marked discrepancies, both because of its symmetrical nature and its pronounced predilection for the female sex. The ratio in infancy was nine females to one male, and at all ages, four females to one male. Furthermore, he considered that the symmetrical form of the Bonnevie-Ullrich syndrome and Turner's syndrome should be classified together.

The characteristics of the symmetrical form were defined by Ullrich (1949) as follows: (1) Webbing of the neck, which at birth was represented by oedematous swelling, and oedema of the extremities which on regression left the skin 'too loose'; (2) moderate dwarfism, hypoplasia of the nipples and sexual immaturity; (3) a low hairline at the nape of the neck and deep-set ears which might show certain degenerative characteristics; (4) frequently epicanthic folds and triangular appearance of the mouth because of the deep-set corners; (5) frequently short and perpendicular nails. (6) There were generally no other web formations nor was there any cranial nerve abnormality. Mental development was normal. (7) Skeletal deformities included an arched palate and cubitus valgus. On radiological examination, mushrooming of the epiphyses and increased digital impressions on the skull were sometimes present. (8) Apart from aplasia of the gonads, involvement of internal organs was rare, although cardiac abnormality such as coarctation of the aorta had been described.

In the case reported above there were sufficient of these features to warrant a diagnosis of the symmetrical form of the Bonnevie-Ullrich syndrome. At her present age there is no evidence of retarded development. An unusual feature of this case is the hypertrophic pyloric stenosis. (This association has not been reported previously, but in one of the cases described by Guinand-Doniol (1947) there was a duodenal stenosis.)

Elevation of the urinary gonadotrophins in patients with primary hypogonadism is not usually found before the age of 10 to 12 years. Silver and Kempe (1953), however, reported an increased level of follicle-stimulating hormone in the urine of a girl of 2 years 8 months who presented the characteristic features of the symmetrical Bonnevie-Ullrich syndrome, ovarian agenesis being confirmed by laparotomy at the age of 4 years.

Although Ullrich had stated that the Bonnevie-Ullrich and Turner's syndromes were associated, it is not clear from a study of the many reports whether all cases of the former have been proved to have hypogonadism. The lack of reports of the Bonnevie-Ullrich syndrome in the English literature compared with the number of cases of Turner's syndrome would suggest that not all those with the

latter condition had peripheral lymphangiectatic oedema in infancy. Further evidence on this point should be easily obtainable from adult endocrinological clinics.

Similarly, ovarian agenesis and webbing of the neck are not invariably associated. It is estimated that a third to a half of the recorded cases of hypogonadism have webbed necks and at least a third of cases of webbing of the neck show hypogonadism (Skjelbred, 1953).

The aspects of webbing and of hypogonadism receive different attention in the European and the American literature. The European attitude, usually based on a young age group, is typified by the association of five conditions in which webbing occurs under the title of the pterygium syndrome (Rossi and Caffisch, 1951). The conditions are (1) bilateral Ullrich syndrome, (2) dystrophia brevicolli congenita (including the Klippel-Feil deformity), (3) pterygonuchal infantilism (Turner's syndrome), (4) unilateral Ullrich syndrome, and (5) congenital pterygoarthromyodysplasia.

Rossi and Caffisch concluded from the aetiology and from the analogy with other syndromes that the pterygium syndrome was hereditary.

American authors, on the other hand, regard Turner's syndrome as a sub-division of a wider complex in which decreased stature is associated with primary gonadal insufficiency and which is to be distinguished from pituitary dwarfism (Albright, Smith and Fraser, 1942). The decreased stature is generally considered to be primordial rather than

of endocrine origin. The majority of American studies are with adult patients.

Finally, it would appear that the time has now arrived when eponyms should be abandoned and a clinical description substituted. It is suggested that pterygolympangiectasia would describe the Bonnevie-Ullrich syndrome which could subsequently become pterygolympangiectatic infantilism when gonadal hypoplasia was established.

Summary

A typical case of the symmetrical form of the Bonnevie-Ullrich syndrome with, in addition, congenital hypertrophic pyloric stenosis, is recorded.

The American and European literature concerning the Bonnevie-Ullrich syndrome and its relationship to Turner's syndrome is discussed.

A new name for the Bonnevie-Ullrich syndrome is suggested.

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